

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	: Kogami et al.
Appl. No.	: 10/523,287
Filed	: February 3, 2005
For	: PROCESS FOR PRODUCING N-MONOALKYL-3-HYDROXYL-3-(2-THIENYL) PROPANAMINE AND INTERMEDIATE
Examiner	: Robert H. Havlin
Group Art Unit	: 1626

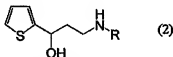
DECLARATION UNDER 37 C.F.R. 1.132

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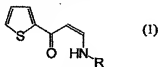
Dear Sir:

I, TAKAHASHI Naoko, declare and state:

I am familiar with the invention claimed in the above-identified application and am familiar with the specification, claims, and prosecution history thereof. These claims are directed to a processes for producing an N-monoalkyl-3-hydroxy-3-(2-thienyl)propanamine represented by General Formula (2):



wherein R is C<sub>1-4</sub> alkyl, comprising the step of reducing a (Z)-N-monoalkyl-3-oxo-3-(2-thienyl)propanamine represented by General Formula (1):



wherein R is as defined above. The claims also are directed to the starting compound, a (Z)-N-monoalkyl-3-oxo-3-(2-thienyl)propanamine represented by General Formula (1).

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2 I have read the Office Actions mailed April 24, 2007 and October 18, 2007, and understand that Claims 4 and 5 have been rejected under 35 U.S.C. § 103(a), as being obvious in view of methyl analogs disclosed in Cassella Farbwerke et al. (CA 88:105153); Singh et al., (CA 115:29157); and Bogdanowicz-Swed et al. (CA 136:118356). Even if the (Z)-N-monoalkyl-3-oxo-3-(2-thienyl)propenamines of the present invention are considered to be obvious variants to the ordinary skilled artisan because of their close structural similarity, I believe that the (Z)-N-monoalkyl-3-oxo-3-(2-thienyl)propenamines set forth in Claims 4 and 5 of the present invention produce distinct results from the known compounds disclosed in the prior art references judging from the results of a document search I conducted, for the following reasons.

3. Properties of (Z)-N-monoalkyl-3-oxo-3-(2-thienyl)propenamines recited in Claims 4 and 5 of the Present Invention. As shown in Claim 1, Example 2, etc. of the present invention, the (Z)-N-monoalkyl-3-oxo-3-(2-thienyl)propenamines set forth in Claims 4 and 5 of the present invention are useful for producing the N-monoalkyl-3-hydroxy-3-(2-thienyl)propanamine represented by General Formula (2). In other words, by reducing the instant (Z)-N-monoalkyl-3-oxo-3-(2-thienyl)propenamine, the above-mentioned N-monoalkyl-3-hydroxy-3-(2-thienyl)propanamine can be directly or easily obtained. In the reduction reaction, for example, the reaction for producing the N-methyl-3-hydroxy-3-(2-thienyl)propanamine, which corresponds to the N-monoalkyl-3-hydroxy-3-(2-thienyl)propanamine represented by General Formula (2) wherein R is a methyl, using (Z)-N-methyl-3-oxo-3-(2-thienyl)propenamine, which corresponds to the (Z)-N-monoalkyl-3-oxo-3-(2-thienyl)propenamines of Claims 4 and 5 of the present invention wherein R is a methyl, is shown below.

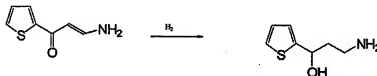


4. 3-amino-1-(2-thienyl)-2-propen-1-one disclosed in Cassella Farbwerke, et al. (CA88:105153). I conducted a document search of prior art disclosing the reduction of 3-amino-1-(2-thienyl)-2-propen-1-one, specifically applying the CAS No.65653-29-4 of the 3-amino-1-(2-

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thienyl)-2-propen-1-one. I conducted an AND search using CAS No.65653-29-4 and keywords including "Reduction", "Hydrogen", "Hydrogenation" or synonyms thereof in "Chemical Abstracts" (CA V.1-V.147(21):1907.01.01-2007.11.13) using STN (The Scientific and Technical Information Network). However, there were no search results found.

5. I next conducted a document search regarding 3-amino-1-(2-thienyl)propanol, which can be obtained by reducing 3-amino-1-(2-thienyl)-2-propen-1-one and is considered to be a variant of the N-monoalkyl-3-hydroxy-3-(2-thienyl)propanamine; similarly, the N-monoalkyl-3-hydroxy-3-(2-thienyl)propanamine represented by General Formula (2) is obtained by reducing the (Z)-N-monoalkyl-3-oxo-3-(2-thienyl)propanamine of Claims 4 and 5 of the present invention. Here, the reaction using 3-amino-1-(2-thienyl)-2-propen-1-one is as shown below.



Specifically, the document search was conducted in the following manner. A search using 3-amino-1-(2-thienyl)-2-propen-1-one and the production method of 3-amino-1-(2-thienyl)propanol (CAS Nos. 858130-53-7, 65653-31-8) was conducted in the same manner as described above. However, there were no results found. For verification, a document search regarding methods for producing 3-amino-1-(2-thienyl)propanol was conducted in the same manner as described above. Two documents were found (one patent document and one non-patent document), but no documents disclosed a method for reducing the 3-amino-1-(2-thienyl)-2-propen-1-one in the abstract. Based on the results of the document search, I believe that directly or easily obtaining 3-amino-1-(2-thienyl)propanol by reducing 3-amino-1-(2-thienyl)-2-propen-1-one is unobvious for a skilled artisan.

6. By comparing the structural formulae, it becomes very clear that the Compounds [2] to [4] disclosed in the three prior art references cannot be used as a material for directly obtaining N-monoalkyl-3-hydroxy-3-(2-thienyl)propanamine. I also conducted a similar document search to confirm that our argument is correct. Specifically, I conducted an AND search using 3-amino-1-(2-thienyl)-2-propen-1-one and the method for producing the N-methyl-

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3-hydroxy-3-(2-thienyl)propanamine represented by General Formula (2) wherein R is a methyl. However, there were no results found.

7. In order to obtain the N-monoalkyl-3-hydroxy-3-(2-thienyl)propanamine represented by General Formula (2) from 3-amino-1-(2-thienyl)-2-propen-1-one, it is clear from the comparison of the structural formulae of the two compounds that attaching an alkyl to a nitrogen atom is a necessary step. Therefore, even if there was any prior art teaching that N-monoalkyl-3-hydroxy-3-(2-thienyl)propanamine can be produced using 3-amino-1-(2-thienyl)-2-propen-1-one, persons having ordinary skill in the art could not, from common general knowledge, directly or easily produce the N-monoalkyl-3-hydroxy-3-(2-thienyl)propanamine represented by General Formula (2), by reducing 3-amino-1-(2-thienyl)-2-propen-1-one.

8. 3-amino-1-(2-thienyl)-2-buten-1-one disclosed in Singh et al (CA 115:29157) and 3-dimethylamino-1-(2-thienyl)-2-propen-1-one disclosed in Bogdanowicz-Szwed et al. (CA 136:118356). Similar to the searches described in paragraphs 4-7 above, document searches of prior art were conducted relating to the reduction of 3-amino-1-(2-thienyl)-2-buten-1-one disclosed in Singh et al (CA 115:29157) and 3-dimethylamino-1-(2-thienyl)-2-propen-1-one disclosed in Bogdanowicz-Szwed et al. (CA 136:118356). However, there were no results found.

9. Conclusion. As described in paragraphs 4-8 above, 3-amino-1-(2-thienyl)-2-propen-1-one, 3-amino-1-(2-thienyl)-2-buten-1-one and 3-dimethylamino-1-(2-thienyl)-2-propen-1-one, which are known compounds disclosed in the prior art references, and which are considered to be variants of the (Z)-N-monoalkyl-3-oxo-3-(2-thienyl)propenamine of Claims 4 and 5 of the present invention, cannot be used for producing variants of the N-monoalkyl-3-hydroxy-3-(2-thienyl)propanamine represented by General Formula (2) by reduction thereof. In conclusion, it is impossible to directly or easily produce the variants of the N-monoalkyl-3-hydroxy-3-(2-thienyl)propanamine from known compounds. In other words, the known compounds neither produce results the same or similar to those of the (Z)-N-monoalkyl-3-oxo-3-(2-thienyl)propenamine described in paragraph 3, nor have properties the same or similar to those of the (Z)-N-monoalkyl-3-oxo-3-(2-thienyl)propenamine.

10. Accordingly, even if the (Z)-N-monoalkyl-3-oxo-3-(2-thienyl)propenamines of Claims 4 and 5 of the present invention are "obvious variants to the ordinary skilled artisan because of their close structural similarity," it produces distinct results from the known

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compounds disclosed in the prior art references, such that it can directly or easily produce the N-monoalkyl-3-hydroxy-3-(2-thienyl)propanamine represented by General Formula (2).

11. In conclusion, the Examiner's rejection on the basis that the (Z)-N-monoalkyl-3-oxo-3-(2-thienyl)propanamines of Claims 4 and 5 of the present invention produce or possess the same or similar properties as those of the compounds disclosed in the prior art references is groundless. The inventions of Claims 4 and 5 of the present application are unobvious from the three prior art references.

12. I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful, false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful, false statements may jeopardize the validity of the application or any patent issued thereon.

Date: 2008. 1. 24.

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